EVENT ABSTRACT

Back to Event

Divergent functional network deficits during an attention-executive task in Lewy body dementia and Alzheimer's disease

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Introduction: Core symptoms of patients with Lewy body dementia are fluctuations in cognition with marked attentional dysfunction. However the neuroanatomical underpinnings of these are insufficiently understood, which impedes the development of specific therapeutic strategies. As neurodegenerative disorders are not only impairments of discrete brain areas, but can also be seen as disorders of brain networks or disconnection syndromes (Morrison et al., 1986), we aimed to investigate underlying network dysfunctions during attentional processing in Lewy body dementia and compare these with Alzheimer's disease and healthy controls.

Methods: We used event-related functional magnetic resonance imaging to examine functional connectivity in 30 patients with Lewy body dementia, 20 patients with Alzheimer's disease, and 21 age-matched healthy controls during an event-related attentional task. All subjects performed a modified version of the Attention Network Test (Fan et al., 2002), where they were instructed to press a button in response to the majority direction of arrows that were either directed all in the same direction (congruent) or with one arrow pointing in the opposite direction (incongruent).
After preprocessing, network activations were extracted by an Independent Component Analysis, fMRI data were temporally concatenated across all participant groups and common activations were derived with FSL-MELODIC (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/MELODIC), which inferred 37 networks. We visually selected five networks (executive network, ventral and dorsal attentional network, default mode network) for further analysis. Then we extracted subject-specific time-series of each network of interest using FSL's dual regression tool (Beckmann et al., 2009). Separate GLMs were performed for the time-course for each subject and network with each individual event as a separate regressor. The resulting beta estimates were grouped as beta series and correlated between the networks to derive information about functional network interaction (Rissman et al., 2004). We compared the resulting covariance matrices between groups, using FSLNETs (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSLNets) and custom Matlab (Mathworks, Natick, Massachusetts) scripts.

Results: Our study revealed that functional connectivity of ventral and dorsal attention networks was reduced in patients with Lewy body dementia compared to patients with Alzheimer's disease and healthy controls during all conditions, although most prominently during incongruent trials. On the contrary, Alzheimer's disease was dominated by hyperconnectivity between the posterior part of the default mode network and the dorsal attention network in all conditions, particularly during incongruent trials.

Discussion: We suggest that the reduced connectivity in Lewy body dementia is mainly driven by a failure of bottom-up ventral attention networks, which leads to an over-reliance on the top-down dorsal attention network. The observed hyperconnectivity in Alzheimer's disease might be either a compensatory effect to surmount default mode network dysfunction (Firbank et al., 2016) or a sign of the disturbed transition of the default mode network from rest to task.

Our study shows dementia syndromes can consist of both hypo- and hyperconnectivity of distinct brain networks, contingent upon on the respective cognitive demand and available neural resources. Due to different underlying pathologies, these functional connectivity changes differ between Lewy body dementia and Alzheimer's disease and this might be of relevance for focussed cognitive therapies.

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